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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/125,747	08/25/98	TOROSSIAN F	TORO-0101-PU

HM12/1222

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	8

DATE MAILED: 12/22/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/125,747	Torossian
Examiner	**Group Art Unit**
S. Devi, Ph.D.	1641

☒ Responsive to communication(s) filed on *Nov 24, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-8* is/~~are~~ pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-8* is/~~are~~ rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☒ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: *96 02445 filed 02/26/96 in France*.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1) The instant application has been filed under 35 U.S.C § 371 as a 371 application of the PCT application PCT/FR97/00334, filed 02/25/1997, with a priority claim to an earlier application, 9602445, filed 02/26/96 in France.

Preliminary Amendment

2) Acknowledgment is made of Applicant's amendment filed 11/24/99 (paper no. 7).

Election

3) Acknowledgment is made of Applicant's election of invention I, claims 1-6, filed 11/24/99 (paper no. 7) in response to the written lack of unity mailed 10/04/99 (paper no. 5). Applicant has not traversed. Applicant contends that claim 8 has been amended to correct its dependency. Applicant states that claim 7 (reciting an "anti-...immumodulatory and vaccine complex") relates to a specific packaging of the immumodulatory and vaccine complex "according to claims 1-6" and requests that claims 7 and 8 be combined with invention I. Since Applicant has clarified that "anti-...immumodulatory and vaccine complex" recited in claim 7 is the complex of claims 1-6, the two invention groups have been rejoined and examined together.

Status of Claims

4) Claims 1-8 are pending in this application and are under examination. An Action on the Merits for these claims is issued.

Information Disclosure Statement

5) Acknowledgment is made of Applicant's Information Disclosure Statement filed 08/25/98 (paper no. 3). The information referred to therein has not been considered, because the documents are not translated to English.

Abstract

6) This application does not contain an abstract of the disclosure as required by 37 C.F.R 1.72(b). An abstract on a separate sheet is required. As this application has been filed under 35 U.S.C § 371 with a priority claim to PCT/FR97/00334, it is suggested that Applicant copy the abstract of PCT/FR97/00334 for submission in order to avoid any NEW MATTER issues.

Specification - Informalities

7) The instant application is informal in the format or arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the Applicant's use.

Content of Specification

(a) Title of the Invention: See 37 C.F.R 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.

(b) Cross-References to Related Applications: See 37 C.F.R 1.78 and M.P.E.P. § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See M.P.E.P. § 310.

(d) Reference to a "Microfiche Appendix": See 37 C.F.R 1.96(c) and M.P.E.P. § 608.05. The total number of microfiche and the total number frames should be specified.

(e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 C.F.R 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 C.F.R 1.74.

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 C.F.R 1.71. The description should be as short and specific as is necessary to describe the invention adequately

and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 C.F.R 1.75 and M.P.E.P. § 608.01(m). The claim or claims must commence on separate sheet. (37 C.F.R 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 C.F.R 1.81, 1.83-1.85, and M.P.E.P. § 608.02.

(l) Sequence Listing: See 37 C.F.R 1.821-1.825.

8) The specification of the instant application is objected to because:

(a) The names of bacterial species in the specification are not italicized. See for example: page 9, lines 3-9. To be consistent with the practice in the art, the names of all bacterial species in the instant disclosure be italicized. It is suggested that Applicant review the entire specification as this is only an example of such an error. Applicant is cautioned about the entry of new matter when amending the specification.

(b) The names of several bacterial species in the specification are misspelled. For example, "pyrogenes" on page 4, line 22 should be "*pyogenes*". "Staphilococcus" on page 4, line 23 should be "*Staphylococcus*". "Hemophilus" on page 4, line 29, should be "*Haemophilus*". It is suggested that Applicant review the entire specification as these are only a few example of such errors. Applicant is cautioned about the entry of new matter when amending the specification.

(c) Some of the prior art references cited in the specification lack full publication details. For example, see page 14, line 12: "VENNEMAN et al." Correction is required.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

9) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making

and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10) Claims 1-8 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description and as failing to provide an enabling disclosure.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

First, instant claims contain subject matter which is not described in the specification in such a way as to enable one skilled in the art to make and/or use, i.e., practice the invention and the full scope of the invention. The specification does not provide a clear written description of "specific therapeutic immunomodulatory complex" (claim 1), "anti-Helicobacter-specific immunomodulatory and vaccine complex" (claim 7), "a functional amino acid arm, ensuring binding to a target, with a genetic RNA arm corresponding to the coded description of the composition of the functional arm" (claim 1), and the immunomodulatory complex being used "as an anti-idiotype vaccine against the idiotypes of anti-bacterial antibodies which make it possible to avoid, in particular, recidivations of the initial digestive tract pathology" (claim 5). Further, the precise description or meaning of "factors linked to the bacterium" and "factors linked to the host" recited in claim 7 is not provided. The "other products with bacteriostatic, bactericidal or bacteriolytic effects" recited in claim 7 are not exemplified or described. Furthermore, page 13 of the specification recites the collagen type III as the "immunity adjuvant factor", and the complex as containing "amino acid sequences" of the collagen type III. However, claim 3 recites that the amino acids from collagen "are chosen from" the various amino acids recited in the claim. With

this inconsistent description, one of ordinary skill in the art would not be able to understand whether the whole sequence is present in the complex, or any one of the recited amino acids is included in the complex, and therefore would not be able to make and use and/or reproducibly practice the invention without undue experimentation.

Further, the written description does not permit one skilled in the art to determine whether the "immunomodulatory complex" of claims 1-6 and the "vaccine complex" of claims 7 and 8 are two different products, the former being a non-specific adjuvant or a general immunopotentiator, and the latter being a specific "vaccine complex". The specification does not allow one of ordinary skill in the art to grasp the nature of the association between the multiple components present in the "complex". For example, "bacterial membrane fractions" as recited in claim 1 are a mixture of multiple, defined and undefined antigens including lipids, polysaccharides, proteins, glycoproteins, glycolipids etc. It is not described how much of these different components of the "bacterial membrane fractions" should be present in the complex such that the complex can accomplish its alleged therapeutic functions. Further, there is no guidance as to how the "arms" are "coupled" and in what ratio and under what conditions. Description is lacking as to whether the various components are "coupled" covalently or non-covalently, or bound specifically or non-specifically. This information is critical because the art reflects that the nature of association between the various antigenic or adjuvant components has a great impact on the immunogenic potency of each component in a given host. One of ordinary skill in the art would not be able to practice the invention as claimed without undue experimentation due to the lack of description with regard to which part of which bacterial membrane fraction(s) is present in what proportion relative to the "amino acid arm" or the "RNA arm".

Furthermore, no evidence is of record enabling the claimed immunomodulatory complex "as an anti-idiotype vaccine against the idiotypes of anti-bacterial antibodies which make it possible to avoid, in particular, recidivations of the initial digestive tract pathology", for use "against bacterial resistance to conventional antibiotic treatments and the like", or for "eradicating Helicobacter generating pathogeneses by factors linked to the bacterium .... or by factors linked to the host".

Further, the specification fails to set forth sufficient evidence showing that the claimed therapeutic complex could be made and used with **any** "bacterial membrane fractions glycopeptides and/or lipopolysaccharides" in association with the other recited components against "Helicobacter diseases". Note that, as currently claimed, infinite "bacterial membrane fractions glycopeptides and/or lipopolysaccharides" are included in the scope of the claim(s), but no guidance has been provided as to which one or more of the "bacterial membrane fractions glycopeptides and/or lipopolysaccharides" would be critical, or would be required to practice the claimed invention against diseases caused by unspecified species of *Helicobacter*. Furthermore, the immunologic and biologic specificity of "bacterial membrane fractions" and the precise mechanism by which these unspecified "bacterial membrane fractions" accomplish the alleged results, i.e., of being effective against "bacterial resistance", "recidivations of the initial digestive tract pathology" and "Helicobacter generating pathogeneses", is undisclosed. The aetiology (i.e., microbial or bacterial or non-microbial or auto-immune) of the "recidivations of the initial digestive tract pathology" is neither recited in claim 5, nor described in the specification. There is no evidence that the subjects of Examples 2-4, who were treated with the complex of the instant invention, were effectively treated against *Helicobacter*-induced gastritis or duodenal ulcer, because there is no disclosure about the actual aetiology of gastritis or duodenal ulcer in these subjects. Further, it is not disclosed which resistant bacteria, among a myriad of bacteria encompassed in the scope of the claim(s), the immunomodulatory complex is effective against.

In sum, the actual invention is not described in such a way that one skilled in the art could grasp the invention and make and use the invention and/or reproducibly practice the invention with a reasonable expectation of success without undue experimentation. The breadth of instant claims is not commensurate in scope with the enabling disclosure or evidence. In the absence of specific guidance and evidence, instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

11) The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

12) The claims of the instant invention are very poorly written. Applicant is asked to pay close attention to the following comments and suggestion in amending the claims.

13) Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claim 1 is vague in the recitation "[s]pecific" therapeutic immunomodulatory complex, because it is unclear what is this specificity directed to. Note that the specification on page 1, first paragraph, recites that the complex comprises "nonspecific antigens".

(b) Claim 1 is vague in the recitation "coupling", because it is unclear whether this coupling is covalent or non-covalent , and whether it represents specific or non-specific association. Clarification is required. "Coupling" may be interpreted to have multiple meanings in the claim, for example, specific or immunochemical coupling, or non-specific static coupling.

(c) Claim 1 lacks antecedence for the recitation: "**the** ribonucleic acids (see line 9) (Emphasis added), because the earlier recitation in the claim is of "a genetic RNA arm" (see line 5), but not of "ribonucleic acids (RNA)".

(d) Claim 1 is indefinite in the recitation "hepaticus, coronari" (see line 11), since there are no such "strains". Does Applicant mean to recite --*Helicobacter hepaticus, Helicobacter coronari*--?

(e) Claim 2 lacks antecedence for the recitation: "**the** amino acids (see line 2) (Emphasis added). Claim 2 depends from claim 1, which recites "amino acid arm", but not "amino acids".

(f) Analogous criticism as explained above in paragraph (e) applies to claim 3.

(g) Claim 3 is indefinite in the recitation: amino acids from collagen are "chosen from the following group" (see lines 2 and 3), because it is unclear whether the recited amino acids are intended to be Markush species. If Applicant intends a Markush format, the Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" rather than "or" in listing species.

(h) Analogous criticism as explained above in paragraph (g) applies to claim 1.

(i) Claim 4 is vague in the recitation of "treatment of diseases caused by Helicobacter bacteria, by the production of antibodies and the production of endogenous interferon" (see line 4), because it is not clear what diseases caused by what *Helicobacter* species are treated in which host by the production of antibodies to what antigenic component of which helicobacterial species. Are antibodies produced against any antigenic component of any *Helicobacter* species therapeutic against diseases caused by any species of *Helicobacter*?

(j) Claim 6 is indefinite in the recitation "and the like" (see line 3), because it is unclear what is encompassed in this recitation.

(k) Claim 7 is indefinite in the recitation "and the like" (see line 8), because it is unclear what is encompassed in this recitation.

(l) Claim 8 is indefinite for being in an improper Markush format in reciting various routes. The Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" rather than "or" in listing species.

(m) Claim 7 is indefinite for being in an improper Markush format in reciting various antisecretory agents and the factors linked to the bacterium. The Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" rather than "or" in listing species.

(n) Claim 1 is confusing in the recitation "functional amino acid arm ensuring binding to a target", because it is unclear which arm (amino acid or RNA) is ensuring binding to which target. What is encompassed in the "arm" and what constitutes a "functional amino acid arm"? The metes and bounds of "dual molecules" is not clear. What does "a genetic RNA arm corresponding to the coded description of the composition of the functional arm" encompass? Clarification is required.

(o) Claims 1 and 7 are confusing in the inconsistent recitations: "immunomodulatory complex" and "immunomodulatory and vaccine complex". The scope and definition of an "immunomodulatory complex" and "immunomodulatory and vaccine complex" is unclear. It is not clear what the differences are, if any, between an "immunomodulatory complex" and "immunomodulatory and vaccine complex". Further, the recitation: "vaccine complex according

to one of the preceding claims" lacks antecedent basis, because the preceding claims do not recite any "vaccine complex".

(p) Claim 5 is vague and confusing in the recitation "anti-bacterial antibodies", because it is unclear which "bacteria" are these antibodies directed against. Note that claim 5 depends from claim 1, the immunomodulatory complex of which comprises materials from multiple bacteria: *Helicobacter* sps. or *Campylobacter* and the generically recited "bacterial membrane fractions glycopeptides and/or lipopolysaccharides".

(q) Claim 7 is indefinite in the recitation "Anti-Helicobacter-specific immunomodulatory and vaccine complex", because the metes and bounds of this phrase is unclear.

(r) Claims 2-6 and 8 lack proper antecendent basis in not reciting "The" at the beginning of the claims. Correction is required.

(s) It is unclear in what respect claims 4-6, which recite the intended use of the complex, are further limited from claim 1.

(t) In claim 4, are antibodies and endogenous interferon produced *in vitro* or *in vivo*? What is the specificity of these antibodies? Claim 4 depends from claim 1, the immunomodulatory complex of which comprises the ribosomal RNA of selected species of *Helicobacter* or *Campylobacter*. Does any one of these species produce antibodies that can be used in the treatment of diseases caused by any or all species of "Helicobacter bacteria"?

(u) Claim 5 is confusing, because it is unclear how the immunomodulatory complex of any one of claims 1-3 can be used as an "anti-idiotype vaccine against the idiotypes of anti-bacterial antibodies" and how such generic "anti-bacterial antibodies" can "make it possible to avoid, in particular, recidivations of the initial digestive tract pathology". What is meant by "make it possible to avoid" and what are encompassed in the "recidivations of the initial digestive tract pathology"?

(v) In claim 6, it is unclear how the immunomodulatory complex of any one of claims 1-3 can be used "against bacterial resistance to conventional antibiotic treatments", as opposed to antibiotic-resistant bacteria.

(w) Claim 7 is vague in the recitations: "anti-inflammatory agents of the corticoid type", "antisecretory agents, (proton pump inhibitors, of the type including Omeprazole or anti-H2, and the like", "other products with bacteriostatic, bactericidal or bacteriolytic effects, for eradicating Helicobacter generating pathogeneses by factors linked to bacterium (production of various cytotoxins, of inflammation mediators:..". What is meant by "Helicobacter generating pathogeneses by factors linked to bacterium" or "by factors linked to the host"? What "factors" are linked to what bacterium or what host, and how are they linked? What is meant by "a packaging allowing the simultaneous administration" and how does a "packaging" allow "administration?

(x) Claim 7 is vague and indefinite in the recitation "Anti-Helicobacter-specific immunomodulatory and vaccine complex", because it is unclear whether Applicant is referring to an antibody to the complex, or the complex that brings about anti-*Helicobacter*-specific effects or functions.

(y) Claim 8 is confusing in the recitation "Immunomodulatory complex .... characterized by a packaging in the form such that it can be administered by various routes". It is unclear how an immunomodulatory complex can be "characterized by" a packaging, since "packaging" is neither a function nor a physical property of the immunomodulatory complex. It is further unclear how a "packaging" can be "administered by various routes: infusions, intravenous injections, subcutaneous injections, transdermal devices, or per os".

Objections

14) Claims 1 and 3-7 are objected to for the following reasons:

(a) Claim 1 is objected to for the grammatically incorrect recitation "membrane fractions glycopeptides" (see line 7). Correction is required.

(b) Claim 4 is objected to for the superfluous recitation "in particular". It is suggested that Applicant delete this recitation since it serves no purpose.

(c) Claim 7 is objected to for including recitations in parentheses. It is suggested that Applicant use the Markush claim language instead.

(d) Claim 1 is objected to for not italicizing the names of the bacteria and for reciting

incomplete names of the bacteria, i.e., "hepaticus, coronari".

(e) Claim 1 is objected to for reciting the abbreviation "(RNA)" in parentheses in line 9. Note that the recitation "RNA" already appears in line 5 of the claim.

(f) In claim 3, the term "phenylaline" is misspelled.

(g) In claims 4-6, what is encompassed in "its"? For clarity, it is suggested that Applicant delete the term "its", or rewrite the claim using phrases such as "said complex".

Remarks

15) Claims 1-8 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1641 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 a.m to 4.00 p.m. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 1999

James C. Housel
JAMES C. HOUSEL 12/20/99
SUPERVISORY PATENT EXAMINER